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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,259	07/26/2007	Remo Kranich	045463-005000	6454

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EXAMINER	
CORNET, JEAN P	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,259	KRANICH ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-16* is/are pending in the application.

4a) Of the above claim(s) *14-16 (method claims)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-16* is/are rejected.

7)☒ Claim(s) *14-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/09/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. New claims 11-16 are pending for examination. Claims 1-10 have been canceled by Applicant. Claims 11-13 correspond to original claim 3, which is within the elected claims of Group I. Claims 14 and 15 correspond to original claims 8 and 9. New claims 14-16 correspond to the non-elected claims within Groups IV, V and/or VI in the restriction requirement.

Election/Restrictions

2. Applicant's election without traverse of Group I, new claims 11-13 in the reply filed on 4/3/2009 is acknowledged.

Applicant's election with traverse of the election of species requirement in the reply filed on 04/03/2009 is acknowledged. The traversal is on the ground(s) that the genus of compounds presented for examination is more limited than that within original claim 1, the independent claim within Group I. Claims 11-13 does not present a serious burden for examination. This is not found persuasive because the independent claim 11 of Group I has two different core compounds, formula C and D, with the OH and the X' groups in different position of the benzene ring. Applicant elects compound (48), (5-2-[(2-'3-4'-Trihydroxy-biphenyl-3-carbonyl)-amino]-phenyl}-thiophen-2-yl)-acetic acid on page 38 of the specification that reads on compound of formula (D). However, there is no art on the record for this elected specie that reads on claims 11 and 13-16, compound of formula D and the examiner is expanding examination to compound 4 of page 6. The species claims 11-16, drawn to a pharmaceutical composition. Claims 14-16, drawn to a method of making or a method of using corresponding to Groups IV, V or VI of the restriction are withdrawn by the examiner.

The use claims 14-16 are improper under 35 USC 101, see 101, rejection below, as it can be interpreted as being directed to a method of use or a product as well as a method of making the product. These claims are interpreted as products in this case are under examination on the merits as well regarding product embodiment(s) therein.

When responding to this Office Action, Applicants are requested to supply a complete listing of co-pending and/or related applications for each inventor.

Claim Rejections – 35 USC 112 2nd Paragraph / 35 U.S.C. 101

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14-16 are rejected under 35 USC 112 second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as their invention, and, under 35 U.S.C. 101, for falling to within any of the defined statutory classes of patentable subject matter.

Claims 14-16 are "use claims." They provides for the "[u]se of compounds having the structure of formula C or D as defined in claim 11 for the preparation of a medicine for the treatment of a patient, inhibiting the binding of P-selectin, L-selectin or E-selectin and for the treatment, diagnosis, or prophylaxis of inflammatory disorders, chonic obstructive pulmonary diseas, acute respiratory ", but, since the claim does not set forth any steps involved in the

purported method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 15 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in a purported method/process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example Ex parte Dunki, 153 USPQ 678 (Bd. App. 1967) and Clinical Products, Ltd. v. Brenner, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Applicant is directed to cancel the claim or amend it so that resides clearly within one of the statutory classes for examination.

Claim Objections

4. Claims 14-16 are objected to because of the following informalities: use of compounds having the structure of formula C or D as defined in claim 1. Claim 1 is canceled. It should be "as defined in claim 11" Appropriate correction is required.

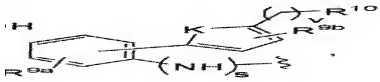
Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether or not K in the thiophen group is K or S in the Y' definition below for the compound of formula C or D. Examiner interprets it as S that reads on the elected species. Clarification is required. In addition, the claims contain so many options, variables, possible permutations and different possibilities of attachment of the different options that lack of clarity because the metes and bounds of the claims can not be determined. For example, there is no definition for CO_2aryl in the specification.



6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement Rejection

Claims 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for the use compounds of formula C and D for the treatment of patient, inhibiting the binding of P-selectin, L-selectin or E-selectin to sle^x or sle^a, does not provide enablement for the prophylaxis of inflammatory disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors:

A. The Nature of the invention

The invention of claim relates to a preparation of compounds of formula C or D for the treatment, diagnosis or prophylaxis of inflammatory disorders. Applicant has no definition for prophylaxis. This term is taken in its plain meaning as preventing.

B. The state of the Art

The Merck manuals online medical library (review/revision August 2006) teach that inflammatory such as Crohn's disease has no cure, but can be treated with certain drugs to relieve symptoms. Also these drugs and surgery can help prevent recurrences, but not preventing the disease.

D. The level of one of ordinary skill

The relative skill in those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

C.) The predictability of the art

The state of the prior art recognizes that the treatment, but not prevention of inflammatory disorders using different drugs and the lack of guidance in the specification remains highly unpredictable.

D) The breath of the claims

The breath of the claims is that the instant compound. for preparing a medicament for the prophylaxis of inflammatory disorders. Thus, the claims taken together with the specification imply these compounds will prevent inflammatory disorders.

E) The amount of direction or guidance provided

Applicant's specification has no working examples demonstrating prevention of inflammatory disorders nor do they provide any guidance demonstrating how one of skill in the in the art would prevent a disease that heretofore was previously unrecognized by those of skill in the art to be able to prevent. Examples of treatment of the effect on inflammatory disorders and their related symptoms are not disclosed.

In light of the recognition of the complexity and nature of the symptom of inflammatory disorders, administration of a compounds would alleviate the symptom, but not the prevention of biological response of vascular tissues to harmful stimuli, and the fact that Applicant has no working examples demonstrating prevention of the symptom of inflammatory disorders, it would be unpredictable and require an undue amount of experimentation for one of skill in the art to practice the full scope of Applicant's claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

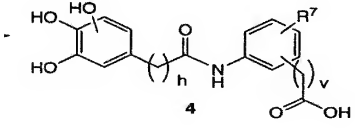
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11, 12, 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blaakmeer et al. (Structure-Activity relationship of isolated avenanthramide alkaloids and

synthesized related compounds as oviposition deterrents for Pieris Brassicae, Journal Of Natural Products, Vol. 57, No. 8, pp. 1145-1151, August 1994) cited in 892 form in view of Appledoorn et al (Rational Optimization of a short Human P-selectin-binding Peptide leads to nanomolar affinity antagonists, The Journal of Biological Chemistry Vol. 278, No. 12, issu of March 21, pp. 10201-10207, 2003) cited in the IDS and Patani et al. (Bioisosterism: A Rational Approach in Drug Desing, Chemical Rev., 1996, 96 (8), 3147-3176) cited in the 892 form

The instant application is drawn to a pharmaceutical composition comprising at least one of the formula C or D and a pharmaceutically acceptable carrier which is useful in a medicine.



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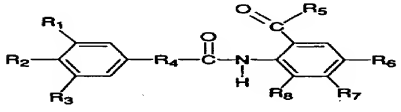
With v is 2, R7 is H and both substituents can be anywhere on the ring..

Blaakmeer teaches structure-acitivity relationship investigation of several compound isolated from the eggs of Pieris brassicae, large cabbage butterfly and eight synthesized related compounds as ovposition deterrents for the insect where their activities were tested. The specie

compound 10, 2-[(3,4,5-trihydroxy-benzoyl)amino}-3,5-dihydroxybenzoic acid of the general formula below (Abstract and page 1146).



Where R1, R2 and R3 are OH; R4 is CH_2=CH_2; R5 is OH; R6 is OH; R7 is H and R8 is OH then the species of this compound is compound 10(page1146), then Blaakmeer's compound reads on the instant claim compound of formula C, when the carboxy goup with the (CH2)v is on the carbon positioned to the left of the amino group and R7 is anywhere of the instant compound.

Blaakmeer does not teach a pharmaceutical composition using the compounds of his invention and a pharmaceutically acceptable carrier.

Appledoorn teaches pentapeptide core motif as potent antagonists for P-selectin using two-step combinatorial chemistry approach. These pentapeptides compounds with gallic acid-substituents proved to be potent inhibitors of P-selectin binding. A dedicated library of peptides derivatives was generated by introducing seven substituents at the N and C termini of the motif. The length and rigidity of the connective spacer can be varied (abstract). These compounds with the number of exposed hydroxyl groups on the first ring appear to be critical for its affinity, because mononbenzoic acid derivatized and dihydrobenzoic acid derivatized were much less effective

than the trihydroxylated counterparts (page 12205 left column last paragraph). P-selectin antagonists were screened for intervention of inflammatory disease (page 10202, results)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the compounds taught in Blaakmeer using combinatorial chemistry as suggested by Appledoorn as P-selectin ligands since Patani suggests monovalent substitution by hydroxyl group in place of hydrogen has recently been used in drug design (page 3152, table 9).

It would have been obvious as well to formulate a pharmaceutical composition to include a pharmaceutical acceptable carrier system such as solvents, and other conventionally known adjuvants since it is well know in the art when making a pharmaceutical composition to include a carrier for drug delivery and since Appledoorn teaches that these ligands offer great therapeutic potential and would greatly benefit from further optimization studies. The technique and skill for adding and selecting a carious materials are well within the level of the ordinary skilled artisan and commonly practiced in the state of the art and thus, obvious absent evidence to the contrary.

One would have been motivated to combine the references and modify the compounds via combinatorial chemistry with reasonable expectation of success, because they share the same core structures that is three hydroxyls groups on the ring with a peptide bonds, and pertinent to the problem which applicant concerns about. MPEP 2141.01 (a).

Conclusion

8. No Claims allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614